Endotracheal Tube Adaptor

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Table of Contents:

Abstract

If an anesthetized patient becomes asthmatic during surgery, albuterol must be administered into the ventilation circuit through an endotracheal tube adaptor to alleviate symptoms. This semester we expanded upon our work from the previous semester by making several design changes to the nozzle and body of our original prototype to help address problems with the spray pattern, ease of commercialization (injection molding), and universality of the adaptor. Laser diffraction and UV Spectroscopy experiments were performed to give a quantitative comparison between the old and new prototypes and other existing technologies. These tests showed that our original prototype generated a higher percentage of desirable small particles in the size range of 5-10 μm, and that it also deposited a higher percentage of albuterol in comparison to the new prototype and other devices. In conclusion, the functional changes we made were detrimental to our prototype's performance while the structural changes provided a viable commercial product.

Background

Introduction

Asthma affects more than 20 million people in the US alone and over 300 million worldwide. It is a frightening and occasionally life-threatening condition in which the bronchi constrict due to an external stimuli, reducing the volume of air an individual is able to inhale with each breath (see Fig. 1 below). Fortunately, asthma symptoms may be controlled in one of two ways: a fast-acting β2-agonist for acute attacks or steroidal medications for chronic relaxation of the bronchioles (Proventil, 2009). Of the many different stimuli which can trigger an attack, the most common are allergies, certain medications, and increased levels of psychological stress. During surgery, each and every one of these risk factors is increased significantly, leading to a dramatically increased probability of an acute asthma attack in an anesthetized patient. If an acute asthma attack occurs during surgery while a patient is intubated with an endotracheal tube, the consequences may be dire since it is nearly impossible to deliver fast-acting bronchodilators to the lungs while an endotracheal tube is in place.

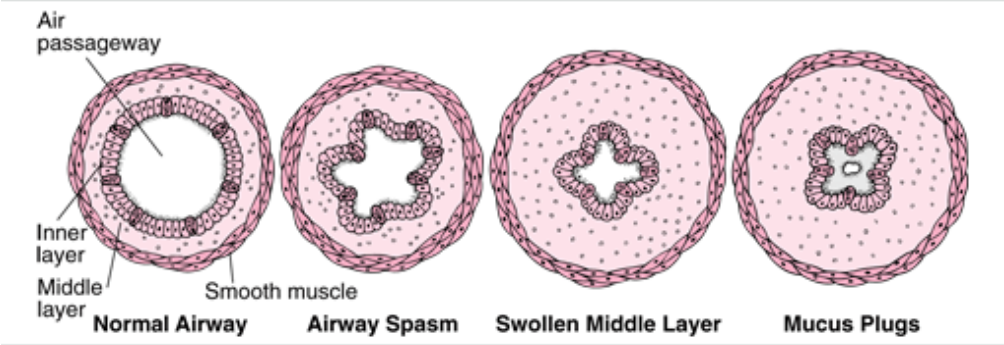

Fig. 1. Depiction of the air passageway during an asthma attack. This constriction makes breathing extremely difficult. Fortunately, fast-acting bronchodilators are able to alleviate these symptoms. [1]

Albuterol sulfate (or Salbutamol sulfate) is the active ingredient found in most aerosolized asthma medication. It is a selective beta$_2$-adrenergic agonist which causes smooth muscle relaxation in the bronchi, ultimately resulting in bronchodilation and an increased volume of oxygen delivered to the lungs. The empirical formula of albuterol sulfate is $(C_{13}H_{21}NO_3)_2 \bullet H_2SO_4$, and its chemical structure can be seen below in Figure 2 (Proventil, 2009). Under normal circumstances, a dose of albuterol from a hand-held Metered Dose Inhaler (MDI)

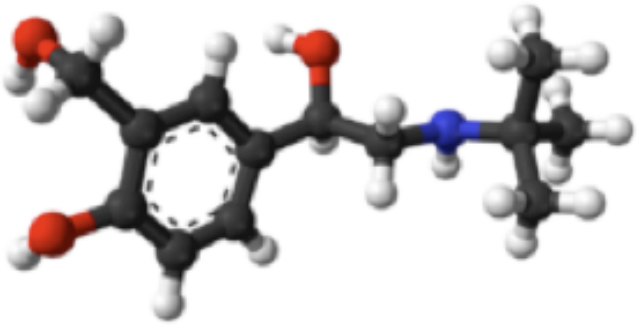

Fig. 2. Chemical Structure of Albuterol [2]

is able to relieve bronchospasms caused by an asthma attack almost instantaneously. An MDI works by delivering a concentrated dose of albuterol (~90μg) from a pressurized canister in an aerosolized mist, which is inhaled deeply into the lungs. Small albuterol particles on the range of 5-10μm are able to travel from the MDI to the trachea and finally to the bronchioles of the lungs. Originally, albuterol canisters came in a standard size. However, the structure of these pressurized canisters was recently modified to include an actuation counter cap. This cap increases a patient's awareness of how many doses remain in the medication canister. The addition of the actuation counter cap is invaluable for patients. However, it poses a compatibility challenge for adaptors that work in conjunction with albuterol canisters.

An anesthesia circuit is completely closed off to all external gas sources to ensure that the patient recieves the correct amount of medication to keep them in a fully anesthetized state (see figure 3 below). If the circuit is opened or diluted with any additional influx of gas, a patient may drift to a lighter state of anesthesia or wake during surgery. This makes it difficult to introduce any additional medication (e.g. albuterol for an asthma attack) unless an adaptor is used as an interface between the circuit and the medication. As mentioned above, albuterol canisters were mechanically modified, which rendered many current adaptors obsolete due to a structurual incompatibility.

Problem Definition

A prototype adaptor was fabricated last semester to act as an interface between all albuterol medication canisters and a closed anesthesia circuit. The adaptor was designed to be compatible with a unique gas sampling female Luer port used during surgery. Initial laser diffraction testing indicated comparable particle size to existing technology available. However, there were concerns over the duration and particle distribution of the spray pattern which our

client wished to address. As a continuation from the previous semester, our original prototype was redesigned with the intention of improving the spray pattern and overall efficacy. We focused specifically on adjusting the nozzle portion of the adaptor in order to reduce aerosolized particle size to 5-10μm in diameter as well as to increase the total amount of albuterol reaching the patient through the distal end of the endotracheal tube. In addition to changing the functionality of the prototype, we also made three non-functional structural changes to improve the ergonomics and aesthetics of our device. The length of the nozzle was reduced from 17 mm to 7.5 mm to ensure universal compatibility with all female Luer ports, the sharp edges on the body of the prototype were rounded to improve patient safety, and draft angles were incorporated into our design to allow for future injection molding.

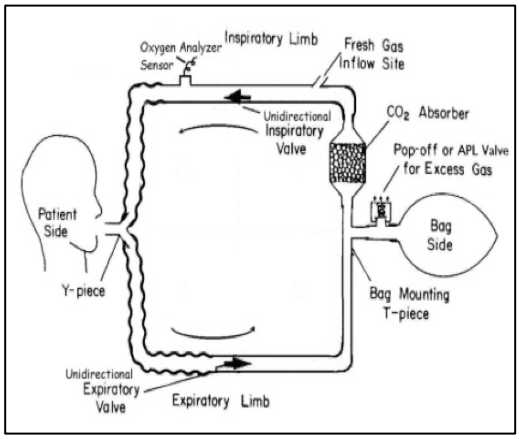

Fig. 3. A closed anesthesia circuit requires an adaptor to deliver asthma medication to an anesthetized patient. [3]

Existing Technology

There are many existing devices used to administer albuterol and other forms of aerosolized medication into an anesthesia circuit. Three devices in particular were very similar in nature to our own: The Bronchodilator Tee, the Nebulizer, and the VBM Tube Inhaler.

The UW-Hospital currently uses the Bronchodilator Tee designed by Boehringer Labs (US Patent #D294298). It has 3 ports; one for the ventilator circuit, one for the endotracheal tube and one that accepts an old style (no actuation counter) medication canister. This device is utilized by numerous hospitals throughout the U.S as it is much easier to use than the nebulizer. However, it is structurally incompatible with the new style of albuterol canister.

The nebulizer is a device used to administer medication to patients in the form of a vapor that is inhaled into the lungs. This device takes medication in a liquid state and passes through gas at a high flow rate, vaporizing the liquid. The allows the medication to travel deeper into the respiratory tract, speeding up its effects. The nebulizer, however, is very inefficient for two

reasons: One, it dilutes the anesthesia mixture reaching the patient and increases their chances of drifting to a lighter state of anesthesia, and two, it requires significantly more liquid medication to do the same job as a smaller dose of concentrated aerosolized medication.

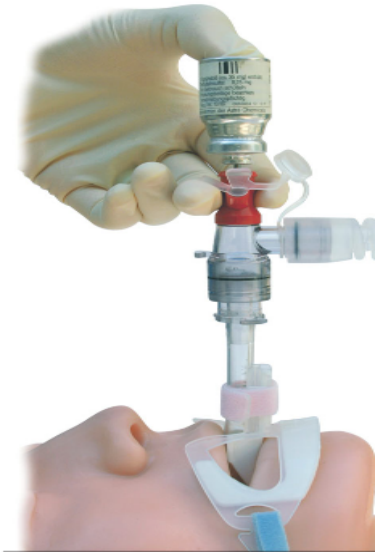

Fig. 4. The VBM Tube Inhaler. [4]

The VBM Tube Inhaler is a brand new device manufactured by Volker-Bertram Medical, Incorporated. Our client discovered this product when he met with the CEO of VBM at the National Convention of Anesthesiology in New Orleans. It is very similar to our prototype in design and allows for the direct administration of Albuterol into an anesthesia circuit through a common elbow. However, this product is also incompatible with the structurally new Albuterol canister. The VBM Tube Inhaler can be seen in figure 4.

Client Requirements

Throughout the course of the semester we met with our client several times to ensure we were focusing on the problems he wished for us to address. The following section lists both the essential design features for the semester as well as the desirable features that weren't absolutely necessary for the completion of our final design.

Essential Features

We defined essential features as the client's requirements that were absolutely necessary for the prototype to achieve basic functionality. These items were considered non-negotiable.

- Spray characteristics: This was the primary feature our client wanted adjusted from the previous semester. The spray pattern of our original prototype was streamlined and occurred over a long time interval. Our client wanted the spray to be changed to a rapid puff which was actuated over a shorter time interval, reflecting the spray pattern of a handheld MDI.

- Nozzle dimensions: Another main feature our client wanted addressed was the length of the nozzle and the diameter of the spray orifice, the former to increase compatibility and the latter to improve the spray pattern.
- Particle Size: Our client desired a particle size range of 5-10µm.

Desirable Features

We defined desirable features as features that our client would like to see addressed but didn't directly affect the adaptor's functionality. These features were ultimately all incorporated into our final design.

- Rounded edges: Our client wanted the sharp edges on the body of the prototype to be rounded off for ergonomic reasons.
- Injection-moldable: Our client wanted the prototype to have the option of being mass-produced through injection molding.
- Actuation Counter: Our client wanted an actuation counter included on the body of our prototype to allow patients to know the number of doses left in the medication canister.

Preliminary Design Ideas

Design Alternative 1: Micro-Filter

The first design alternative, the microfilter, gets its name from the filter-like array of microscopic holes on the end of the nozzle (see figure 5). The holes on most standard microfilters range in size from 10-20 microns. We came up with this idea during a team brainstorming session. After meeting with Professor Reitz (a fluid and aerosol dynamics Professor on campus), we discovered that this is actually the technology used by Glade scent dispensers. These scent dispensers force a liquid fragrance through the microfilter in order to create a cloud of aerosolized mist. The creation of a cloud rather than a jet of aerosolized mist was the main rationale behind this design alternative. The basic concept behind the filter was to take the technology used in the

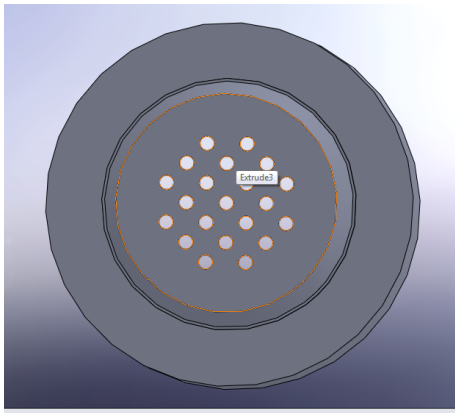

Fig. 5. The microfiliter design employs the use of many holes at the distal end from 10-20µm.

Glade scent dispensers and make it applicable to pressurized medication. To accomplish this, an array of 10-20 μm holes would have to be added to the functional unit of the original prototype. This array of small holes would serve to aerosolize the medication in place of the single 0.25 mm hole on last semester's prototype.

Forcing the pressurized medication through multiple microscopic holes instead of one slightly larger hole would have several advantages. Most importantly, it would consistently generate small particles in the desired size range (5-10 μm in diameter). In addition, this design would alter the spray pattern of our current prototype and create an aerosolized mist. By breaking up the initial stream of medication into many smaller streams, the particle velocity upon leaving the nozzle would be reduced and a mist would be generated. This would substantially increase the percentage of particle deposition in a patient's lungs.

Although the filter design addresses many of the issues with our current prototype, it also has several disadvantages. First, this design would be prone to clogging. Since the filter is created using such small hole diameters, it would only take a small amount of dried medication or any other miscellaneous particles to clog the holes. If too many of the holes begin to clog the pressure required to force the medication through the filter would become too great for the canister to supply, or too great for a plastic adaptor to withstand. This could potentially lead to structural failure, which would have serious health implications for both the patient being treated and the user. This design would also be very difficult and expensive to fabricate. Much of the cost and labor time behind the production of our first prototype resulted from drilling the 0.25 mm hole. By significantly decreasing the hole diameter and increasing the number of holes, this task would become exponentially more difficult and costly.

Design Alternative 2: Spherical Collider

The second design alternative, the spherical collider, was also first though of at a team brainstorming session and confirmed by Professor Reitz. The basic concept behind the spherical collider design is to take the pressurized medication from the canister and collide it with a spherical surface. The collision between the medication and the spherical surface breaks the original stream of liquid into multiple independent streams. These streams travel around the

sides of the sphere and collide on the back end. This second collision helps to aerosolize and disperse the liquid medication (see figure 6).

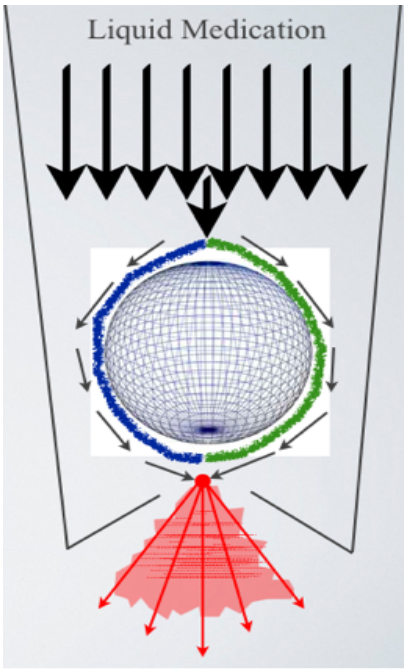

Fig. 6. Illustration of spherical collider

The spherical collision design has three main advantages over our current prototype. First, it would generate small particle sizes due to the consecutive collisions of liquid medication (the first between the medication and the spherical surface, the second between the divergent streams of medication). When two small particles collide their collision breaks each individual particle into several smaller particles. Second, these collisions would also help to create a cloud of mist rather than a stream. The collision of divergent streams of medication would result in a final mist. Third, this design would minimize the chance of particle rain-out on the back of a patient's throat. The multiple collisions of the medication with the sphere and again amongst itself would significantly slow the overall particle velocity. The decrease in velocity associated with the collisions would allow the particles to adequately mix with the anesthesia gases before reaching the patients throat. This in turn would increase the percentage of particle deposition in a patient's lungs.

The first disadvantage of this design is a result of the collision with the spherical surface. Even if this surface is at exactly the optimal diameter and distance from the nipple of the canister, it would be impossible to prevent a significant amount of medication rain-out on the sphere. When the medication collides with the surface, a small portion of it may collect on the sphere. With repeated actuations this could render the sphere useless, or even cause liquid medication to drip into the patient's throat. The second disadvantage with this particular design is that it would also be quite difficult and expensive to fabricate. The added machine cost and time will come from the suspension of a small spherical surface in an already small hole. This will prohibit the machinist from simply boring out the hole using standard drilling techniques and require him to use other more time consuming methods. Finally, the theory behind a

spherical collision is only proven in pure liquids, whereas the medication dispersed from the canister is part liquid and part gas. This may result in the theory not being 100% applicable to our problem.

Design Alternative 3: Contour Taper

Our final design alternative is a forward/reverse taper combination, also known as a contour taper (see figure 7 below). We initially came up with this idea during a team brainstorming session a few weeks into the semester. The idea was reinforced by Professor Rolf Reitz. This design has several distinct advantages which address each of our objectives for the semester.

The contour taper will generate small particles within the desired 5-10 μm range. It will also slow down the particle velocity at the end of the nozzle, thus decreasing the chance that the medication will rain-out on the back of a patient's throat. A contour taper effectively reduces the pressure required to force the medication through the prototype's orifice. This decreases the particle ejection velocity at the distal end of the orifice. This effect can be negated by including a low-pressure area on the backside of the restricted high pressure throat. This was the rationale behind the contour taper. Finally, this design is the most reproducible and the easiest to fabricate. It is the only design alternative that can be injection molded due to the lack of intricate geometry and structural complexity.

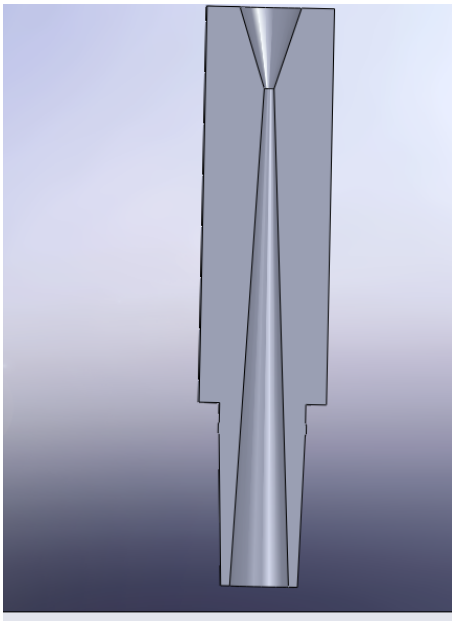

Fig. 7. Preliminary SolidWorks model of the contour taper design.

The main disadvantage of this design is the relative difficulty of fabricating internal tapers. While these tapers can be injection molded, they would be difficult to machine and incorporate in our existing metal adaptor. Relative to the other two proposed designs, the tapers would be the most simple to fabricate.

Final Design

The final design of the new prototype, the contour taper, combined functional, structural, and aesthetic changes to the old prototype in order to achieve this semester's design criteria. The functional changes made focused on addressing the preliminary concerns expressed by Dr. Schroeder associated with the spray distribution and particle size. The general structural changes addressed the ergonomic and commercialization flaws. It was our hope that the combination of these changes would produce a viable, marketable, and ergonomically friendly product to administer albuterol to intubated patients.

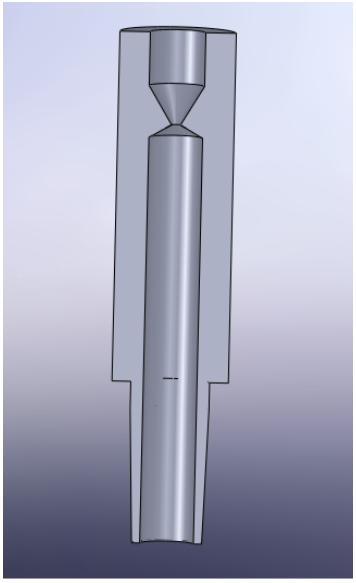

Fig. 8. SolidWorks model of the final contour taper design.

Functional Changes

The first change made to the nozzle of the old prototype was the increase in orifice size (see figures 9 and 10 below). The contour taper model features an orifice size of 0.5 mm, twice as large as the 0.25 mm orifice that was present on the old prototype. The increase in orifice size helped to generate the desired puff of medication by reducing the pressure required to dispense the medication. By increasing the internal cross-sectional area of the prototype, the bottleneck effect was minimized (the clogging of the orifice that occurs when forcing a large volume of medication through a small hole). In addition to the reduction in pressure, the increased orifice size was thought to optimize particle size by adjusting the orifice dimensions to those used in the patient's inhaler (0.5 mm - Tod Connolly - 3M employee).

The most important functional change made to the nozzle of the old prototype was the switch from a standard (forward) taper to a contour (forward/reverse) taper (see figures 9 and 10 below). A contour taper effectively reduces the pressure required to force the medication through the prototype's orifice. This decreases the particle ejection velocity at the distal end of the orifice. According to the textbook Modern Compressible Flow (Anderson, 2003), when a fluid flows from an area of low pressure to a restricted area of high pressure (the throat) the resultant particle velocity is greatly increased as the high pressure forces the particles out of the orifice.

This effect can be negated by including a low-pressure area on the backside of the restricted high pressure throat. This was the rationale behind the contour taper. In our prototype, the throat is defined as the nozzle location with the smallest diameter (the orifice where the liquid medication is aerosolized). By decreasing the particle velocity inside the nozzle with the inclusion of a

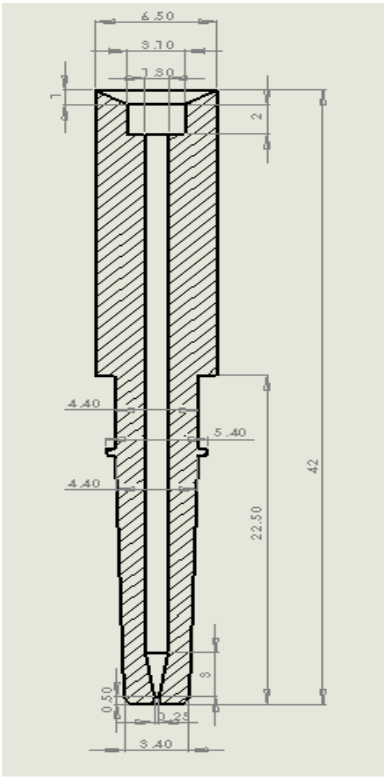

Fig. 9. Dimensions of old prototype nozzle with a 0.25 mm orifice and standard forward taper. All dimensions in mm.

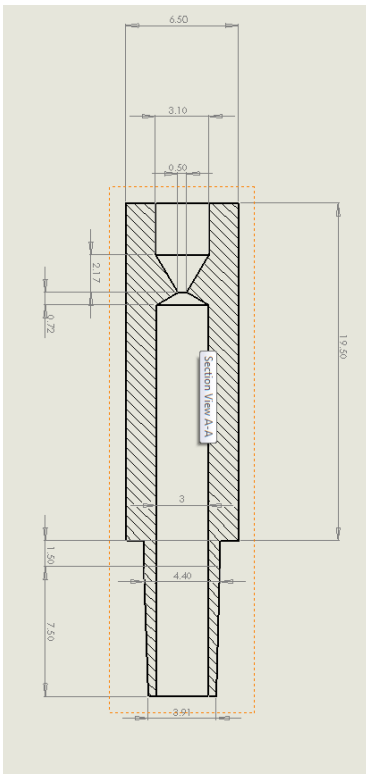

Fig. 10. Dimensions of new prototype nozzle with a 0.50 mm orifice and contour forward/reverse taper combination. All dimensions in mm.

contour taper, it was our hope to deliver a highly concentrated small particle (5-10 microns) cloud of medication into the anesthesia circuit. Obtaining a highly concentrated cloud of small particles is ideal for albuterol administration as it enhances the ability of the medication to mix with the anesthetic gases, ultimately increasing the amount that reaches a patient's lungs. This increase in lung deposition can be attributed to the inverse relationship between the percent of integration into the anesthetic gas and percent medication rainout (the percent of medication lost/ total amount administered per canister actuation).

Structural and Aesthetic Changes

The structural and aesthetic changes made to the old prototype addressed issues associated with commercializing the device. Specifically, after meetings with Tod Connolly and Steve Turch (3M employees who specialize in injection molding) it was determined that our original design was structurally unable to be injection molded. When a molten plastic is forcefully injected to a cast mold, it begins to cool immediately. If the structure doesn't have a uniform thickness, it cools at different rates and is almost impossible to remove from the cast

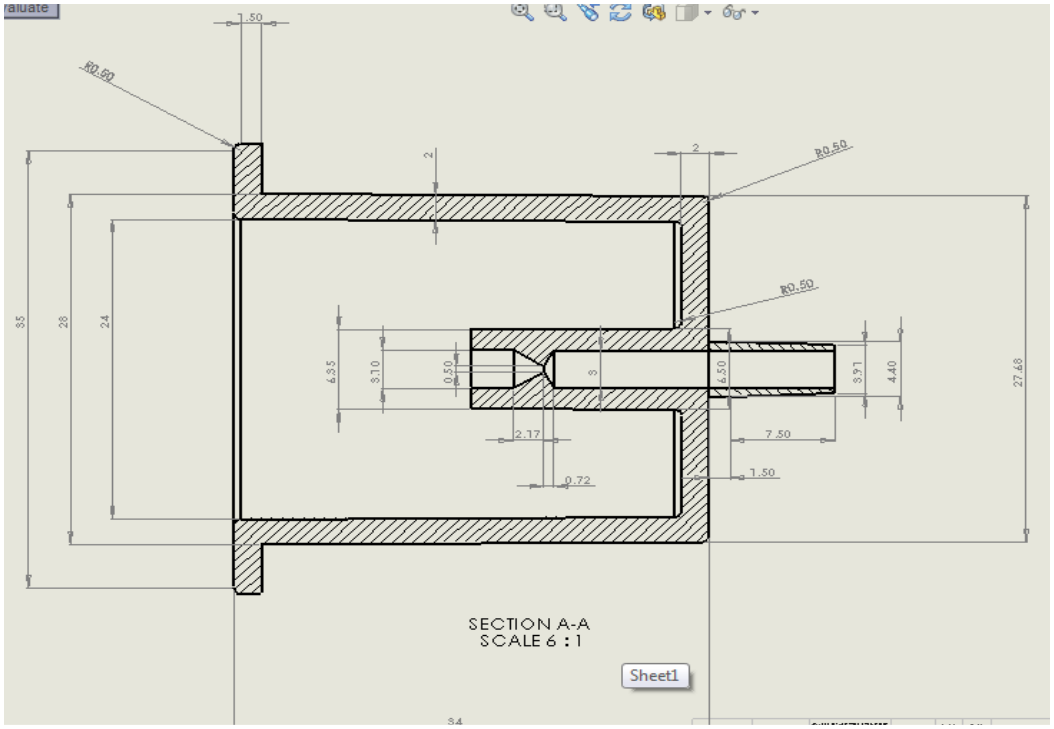

Fig. 11. Solidworks schematic of new prototype with structural and aesthetic changes shown. All dimensions in mm.

with the thicker portions of the wall fully hardened. This can lead to sagging and deformation of the final molded product. To account for this, we incorporated a uniform material thickness in our final design. Along with this, we shortened the nozzle length from 17 mm to 7.5 mm (figure 11). The rationale behind shortening the nozzle was to not only help offset the strong deflection (bending of long narrow holes) forces present during the injection of the plastic, but to also make the adaptor compatible with international Luer standards. Finally, we also made several minor aesthetic changes to our original design - the rounding of sharp edges and the inclusion of an actuation counter.

Testing

Human testing requires FDA 510k approval, which was not feasible for this semester. Instead, two laboratory tests were conducted to characterize the spray pattern of our new prototype and various other devices *in situ*. These tests were used to measure both the quality and quantity of particles reaching the distal end of an ETT when various adaptors are used to deliver albuterol from a pressurized aerosol canister. The aim of this testing was to both validate the efficacy of our new prototype and compare it to both our old prototype and other adaptors.

Laser Diffraction

Laser diffraction is a method commonly used to determine the size of a particle suspended within a gas sample. If the sample is assumed to be homogeneous and representative of the whole solution, the particle size distribution of the sample can be correlated to that of the entire solution. During a laser diffraction test, a laser is projected through a suspended cloud of particles and a collector oriented at 90° to the laser records the various laser deflections (Malvern Instruments). The amount of light collected at the collector element is used to determine the particle size distribution of a sample. Laser diffraction testing is widely accepted as an industry standard in testing aerosol particles, which are often desired to be in the size range of 5-10 μm (Jones *et al.*, Leach *et al.*).

Recent research supports the assertion that bronchodilator dry drug particles (albuterol sulfate, ipratropium bromide, *etc.*) are most effective in controlling bronchospasms when in the size range of <10 μm (Jones *et al.*). Additionally, when a patient uses a personal metered dose inhaler (pMDI or MDI) the amount of albuterol deposited in the lungs rarely exceeds 20% with the majority of the medication "raining out" in the oropharyngeal airway (Leach *et al.*). Smaller particles have the added benefit of traveling more deeply into the lungs than larger particles and thus are highly desirable in dry drug aerosolized medications (Jones *et al.*, Leach *et al.*). In summary, bronchospasms are controlled with a small quantity of high quality particles.

A Malvern laser diffraction system was used to quantify the particle size distribution reaching the end of an ETT using various ETT adaptors (see protocol in appendix). Also, particle size was determined for several adaptors and a MDI without the use of an ETT. Figures

12-15 below summarize the data obtained from the Malvern laser diffraction testing for the old and new prototypes both with and without an ETT. The data obtained on various ETT adaptors (Bronchodilator Tee, 60cc Syringe) and a personal MDI can be found in the appendix (figures 17-19).

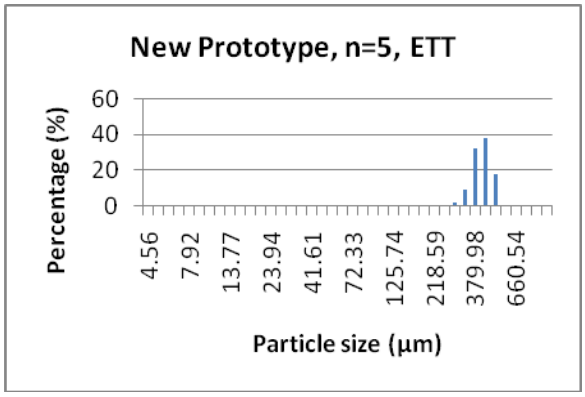

Fig. 12. Average distribution of particle size for new prototype with endotracheal tube, n = 5.

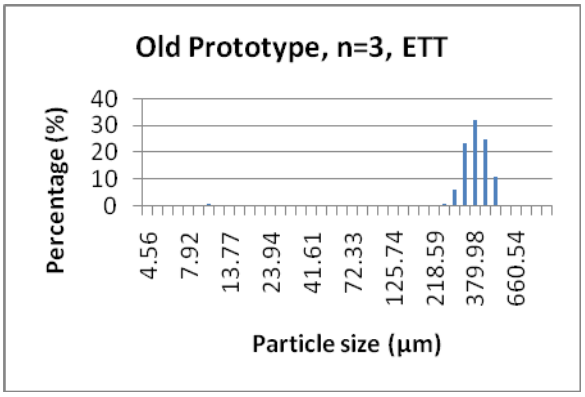

Fig. 13. Average distribution of particle size for old prototype with endotracheal tube, n = 3.

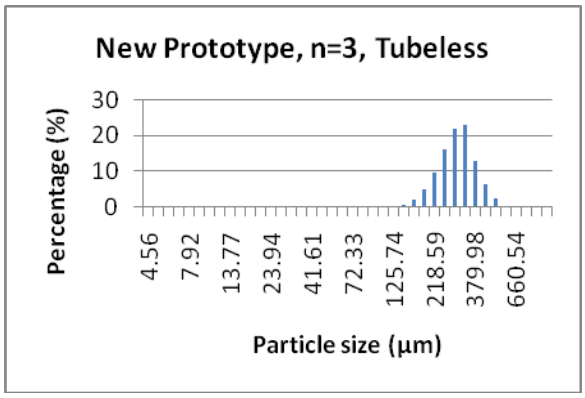

Fig. 14. Average distribution of particle size for new prototype without endotracheal tube, n = 3.

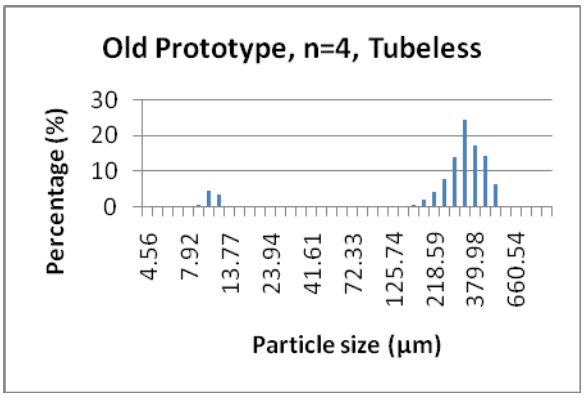

Fig. 15. Average distribution of particle size for old prototype without endotracheal tube, n = 4.

The data from this test indicates that the old prototype was the most effective device in delivering the desired small particles to the distal end of an ETT when compared to the new prototype and other ETT adaptors (see appendix to compare to other ETT adaptors). When comparing figures, it is apparent that the old prototype without an ETT has the largest percentage of small particles (5-10 µm). Additionally, the small particle distribution was very similar when comparing the old prototype without an ETT to a personal MDI which further validates its

efficacy. Multiple trials (at least n=3) were performed and compiled for each test to ensure accurate, reliable data.

UV Spectroscopy

The concentration of a solution can be determined using either photo or ultraviolet (UV) spectroscopy depending upon the unique characteristics of the solution of interest (Reusch). UV and photo spectroscopy tests vary in the wavelength of light used to test the samples. Samples that contain conjugated double bond systems are best suited for UV spectroscopy while samples of a specific visible color are easily tested with photo spectroscopy (Reusch). Albuterol contains a characteristic benzene ring (conjugated double bond system) and thus a solution of albuterol will absorb light in the UV range (NIH). Using the Beer-Lambert law one is able to relate concentration of a solution to the unique absorbance of that solution (at a specific wavelength of light). The absorbance of a solution is defined as the ratio of the intensity of light entering the solution to the intensity of light exiting the solution when traveling a specified distance through the solution (Reusch).

Using UV spectroscopy, the amount (mass) of albuterol leaving the distal end of an ETT was quantified in a solution of sodium hydroxide following a similar protocol to one found in literature (Peterfreund *et al.*). First, standards were made by serially diluting a known concentration of albuterol. The absorbances of these standards were recorded and a standard curve generated (figure 16). Next, following a specific protocol (see appendix), the concentration of albuterol exiting the ETT was determined using various ETT adaptors as well as a personal MDI and from it mass of delivered albuterol was calculated and compared. This test was performed collecting albuterol at the distal end of an ETT with approximately 8 L/min airflow to mimic a clinical setting.

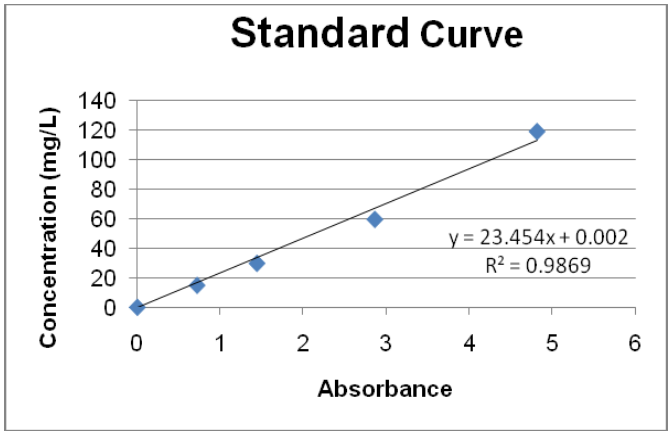

Fig. 16. Standard Curve for UV Spectroscopy test.

Table 1. Data gathered from UV Spectroscopy Experiment comparing absorbance, concentration, mass, and percent delivered of 5 different devices.

Test	Absorbance	Concentration (mg/L)	Mass (µg)	Percent delivered (%)
Old prototype	0.142	3.32	16.61	3.69
New prototype	0.037	0.87	4.33	0.96
MDI (No ETT)	0.842	19.74	98.72	21.94
60cc syringe	0.727	17.04	85.23	18.94
Bronchodilator Tee	0.109	2.57	12.83	2.85

The results (see table 1 above) for this test indicate that the old prototype outperformed both the Bronchodilator Tee and the new prototype when attached to an ETT. However, the 60cc syringe deposited a larger quantity of albuterol through the ETT. But, since quantity of medication is only half the battle in relieving asthma symptoms and larger particles are known to not have as strong of a bronchodilating effect, it is important to look at the quantity of small particles delivered (<50 µm). The MDI was not actuated through the ETT and thus also delivered a significantly larger amount of medication than the other devices.

When the data from the UV spectroscopy test is compared to the percentage of particles less than 50 µm for each albuterol delivering device, another comparison can be made between all devices tested (from laser diffraction test above). By multiplying the mass from each test in table 1 above and the total percentage of particles less than 50 µm from the laser diffraction data one is able to determine the mass of particles less than 50 µm and thus the percent of particles less than 50 µm delivered. These results, summarized in table 2 below, also show that the old prototype outperformed all other ETT adaptors but fell short of the percent of particles delivered by the MDI (which was not attached to an ETT).

Table 2. Data gathered from UV Spectroscopy Experiment comparing mass and percent of particles under 50 µm in size reaching the end of the ETT.

Test	Mass of particles <50 µm (µg)	Percent of particles <50 µm delivered (%)
Old prototype	0.16389087	0.036420193
New prototype	1.9908E-06	4.42401E-07
MDI	5.490317736	1.220070608
60cc syringe	0.000109947	2.44326E-05
Bronchodilator Tee	0.05947988	0.013217751

Ethical Considerations

Human safety considerations

- Small Particle Range:

  Our primary goal from design testing was to obtain the 5-10 μm particle size range for albuterol. Particles in this size range can travel into the lower respiratory tract and have a higher success rate of being inhaled by the patient, reducing the chances of bronchospasms during surgery.

- Abbreviated FDA 510k:

  To obtain market authorization, our product would have to meet the guideline requirements of the abbreviated FDA 510k. To gain this approval, a summary report highlighting all the details must be written and sent for approval. Unfortunately, there were time limitations this semester, and an approval was not filed but will be considered for future work.

Honest Data

- Testing Procedure and Results:

  The testing procedures for each test were carried for each device followed a standard protocol**.** The protocols were written were based on testing procedures carried out in other scientific research papers. Testing procedures for both tests were well carried out as they produced substantial results of the particle size and concentration that the prototype was ejecting. For example, the UV Spectroscopy test produced a coefficient of termination (R-squared value) of 0.98. It also incorporated an air-flow, in efforts to make the test more life-like. One disadvantage for this test is that was only conducted once. Reproducibility of results would have strengthened the conclusions that were from this data. The testing procedures for the Laser Diffraction test were better and more conclusive this semester. This is because the data showed an overall smaller particle size range, some particles even being in the ideal size range. This test could have been

made better by incorporating the International Organization for Standardization's (ISO) methods for particle size analysis using laser diffraction systems.

- Citations:

  Citation of other peoples' work was done efficiently throughout the semester to avoid plagiarism or gaining credit off of other peoples' work. This was especially imperative this semester as the prototype has potential of being patented and care must be taken credit must be given to every source for ideas.

Conclusion

Several functional design changes were made this semester which adversely affected the spray characteristics of our prototype. This was verified from the results we obtained from the two types of testing that were conducted. However, structural changes that were made to the prototype for injection molding purposes were successful and the prototype is now ready for commercialization. Also, a design patent application was formally drawn up and filed with the help of an attorney. Incorporation of elements of the designs from both semesters' work will be taken into consideration to produce a final product that is mass-producible and highly effective at delivering significant amounts of albuterol in the size range of 5-10 μm**.**

Why the prototype didn't work

One main reason that our final prototype did not produce satisfying results was because of the contour taper's angle on the backside of the throat (angle at which the particles leave the orifice of the canister). This angle was immediately after the throat and was very shallow. This could theoretically explain the particles raining out on the sides of the walls of the nozzle and the walls of the endotracheal tube adaptor as well. Another possible explanation is that the reverse taper is not located to the distal end of the nozzle. Moving the taper could in theory reduce the rain out of particles within the nozzle. Moreover, an extremely high pressure drop, which may have also contributed to the excessive rain out, could also have been reduced by the modifications mentioned above.

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Leach, Chet, Gene L. Colice, and Allan Luskin. "Particle size of inhaled corticosteroids: Does it matter?" *Journal of Allergy and Clinical Immunology* 124.6 (2009): S88-93. *ScienceDirect*. Web. 4 Dec. 2009.

"Malvern Instruments | Industrial Laser Diffraction Systems." *Malvern Instruments | Particle Characterization, Laser Diffraction, Rheological and Particle Size Analyzers*. Web. 04 Dec. 2009. <http://www.malvern.com/ProcessEng/systems/laser_diffraction/laser_diffraction.htm>.

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Reusch, William. *Virtual Textbook of Organic Chemistry*. 1999. 16 July 2007. Web. 1 Dec. 2009. <http://www.cem.msu.edu/~reusch/VirtualText/intro1.htm>.

USA. National Institute of Health. National Center for Biotechnology Information. *Albuterol - Compound Summary*. Web. 1 Dec. 2009. <http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=2083>.

Figures

[1] <http://www.merck.com/mmhe/sec04/ch044/ch044a.html>.

[2] <http://en.wikipedia.org/wiki/Salbutamol>.

[3] <http://www.osha.gov/dts/osta/anestheticgases/index.html>

[4] <http://www.vbmmedical.com/p-connectors.html>

Appendix

Laser diffraction figures

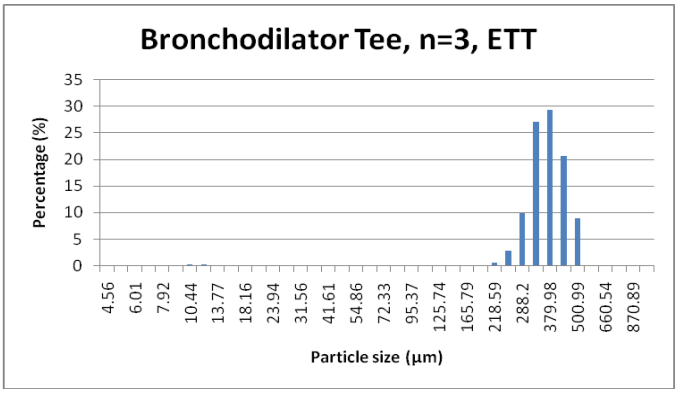


Fig. 17. Average distribution of particle size for bronchodilator tee with endotracheal tube, n = 3.

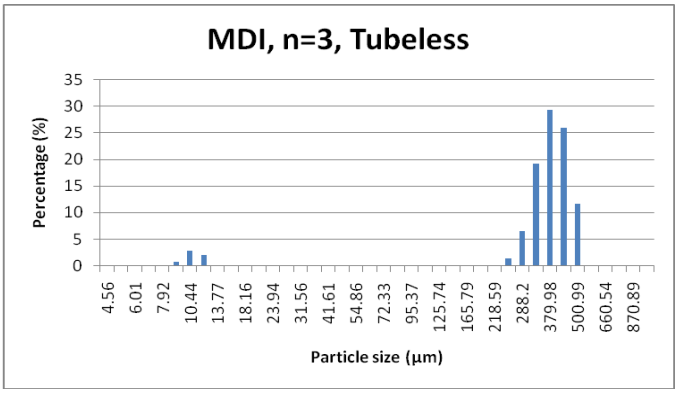


Fig. 18. Average distribution of particle size for MDI without endotracheal tube, n = 3.

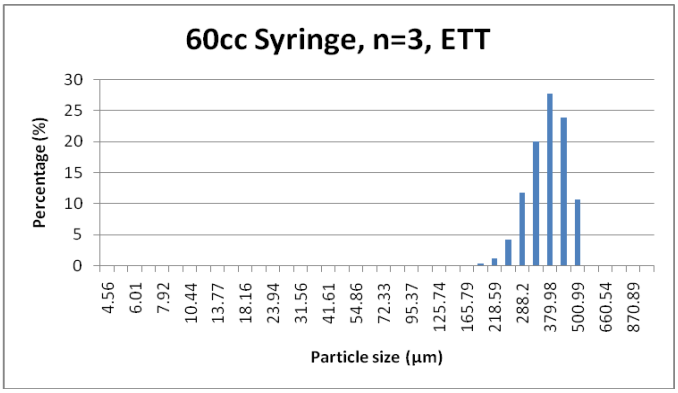


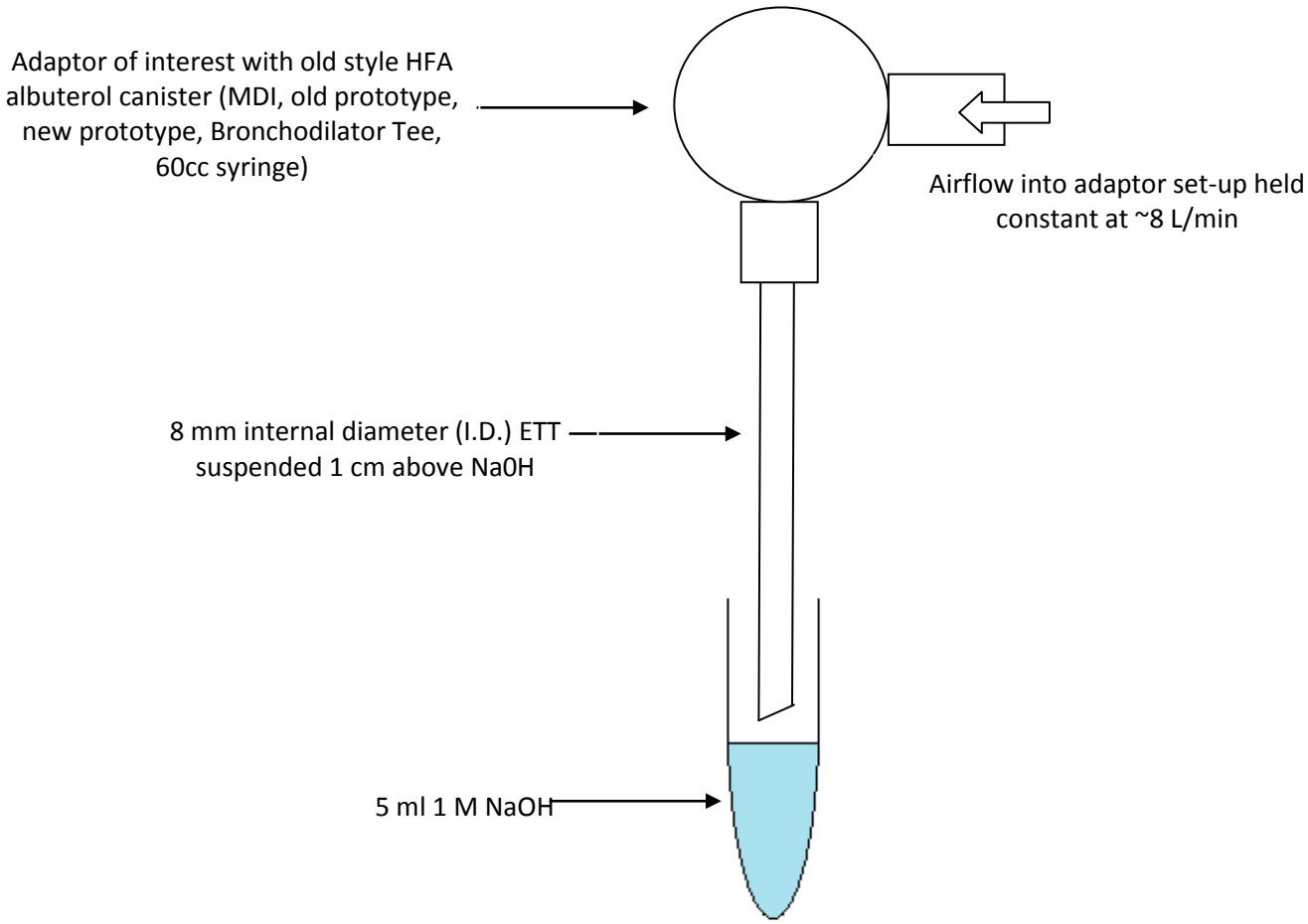
Fig. 19. Average distribution of particle size for 60cc Syringe with ETT, n = 3.

UV Spectroscopy Protocol

Rationale and Experimental Set-up

The concentration of a solution can be determined using either photo or ultraviolet (UV) spectroscopy depending upon the unique characteristics of the solution of interest [2,3]. UV and photo spectroscopy tests vary in the wavelength of light used to test the samples. Samples that contain conjugated double bond systems are best suited for UV spectroscopy while samples of a specific visible color are easily tested with photo spectroscopy [2]. Albuterol contains a characteristic benzene ring (conjugated double bond system) and thus a solution of albuterol will absorb light in the UV range [4]. Using the Beer-Lambert law one is able to relate concentration of a solution to the unique absorbance of that solution (at a specific wavelength of light). The absorbance of a solution is defined as the ratio of the intensity of light entering the solution to the intensity of light exiting the solution when traveling a specified distance through the solution [2].

Using UV spectroscopy, we were able to quantify the concentration of albuterol in a solution of sodium hydroxide [1]. This concentration was determined using various endotracheal tube (ETT) adaptors as well as a personal metered dose inhaler (MDI) and from it mass of albuterol was calculated and compared. This test was performed collecting albuterol at the distal end of an ETT to mimic a clinical setting and the basic set-up of the test is illustrated below.



Materials

- UV spectroscopy software and hardware
- NaOH (1 M)
- 15 ml tornado tubes, pipettor, pipet tips
- 8 mm I.D. ETT
- Airflow capable of 8 L/min
- 2.5 mg albuterol suspended in 3 ml saline solution (for nebulizer), albuterol sulfate HFA aerosol canisters
- Old prototype, new prototype, MDI, 60cc syringe, Bronchodilator Tee
- Aluminum foil

Methods

- Make standard curve of absorbance vs. known concentrations of albuterol using nebulizer albuterol solution (dilute so concentrations will be in range of tested concentration) at 240-245 nm light wavelength
- Test MDI (without ETT), old prototype, new prototype, Bronchodilator Tee, and 60cc syringe using set-up shown above
    - Each test ideally uses new ETT tube as well as a newly primed (5 actuations prior to test) canister of albuterol
    - Use new 15 ml test tube with precisely 5 ml of NaOH for each adaptor tested
- Actuate canister 5 times per test and store albuterol solution protected from UV light (wrapped in aluminum foil) to prevent degradation of albuterol prior to absorbance reading. This allow for a maximum of 0.45 mg albuterol per test (90 mg/L concentration)
- Read the absorbance for each solution and determine concentration using calculated standard curve function. Use the solution concentration to determine other aspects of interest (mass, % dose, *etc.*)

References

[1] Peterfreund, Robert A., Ralph W. Niven, and Robert M. Kacmarek,. "Syringe-Actuated Metered Dose Inhalers: A Quantitative." *Anesth Analg* 78 (1994): 554-58. *Science Direct*. Web. 1 Dec. 2009.

[2] Reusch, William. *Virtual Textbook of Organic Chemistry*. 1999. 16 July 2007. Web. 1 Dec. 2009. <http://www.cem.msu.edu/~reusch/VirtualText/intro1.htm>.

[3] "Ultraviolet-visible spectroscopy -." *Wikipedia, the free encyclopedia*. Web. 01 Dec. 2009. <http://en.wikipedia.org/wiki/Ultraviolet-visible_spectroscopy>.

[4] USA. National Institute of Health. National Center for Biotechnology Information. *Albuterol - Compound Summary*. Web. 1 Dec. 2009. <http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=2083>.

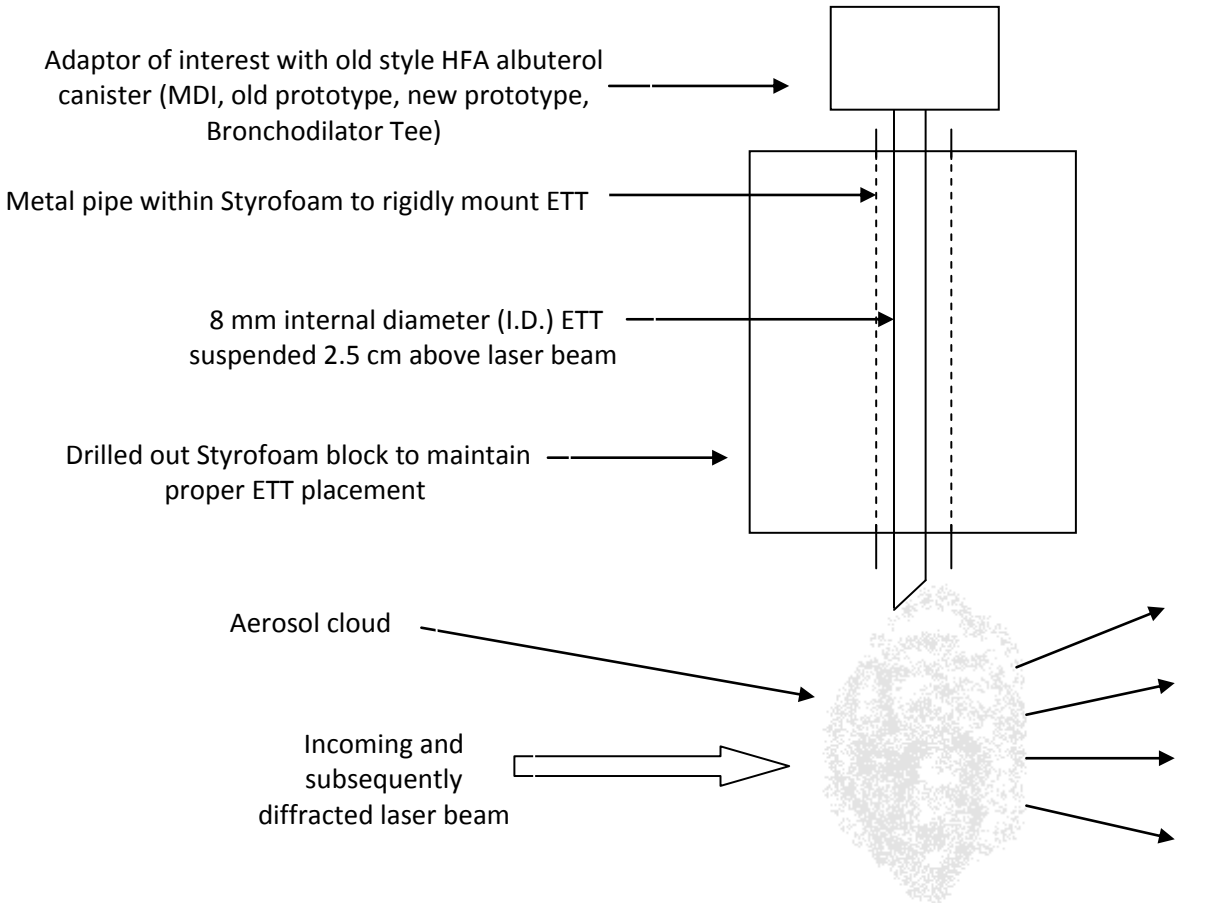
Laser Diffraction Protocol

Rationale and Experimental Set-up

Laser diffraction allows one to determine the size of a particle suspended within a gas sample and, if the sample is assumed to representative of the whole solution, one can correlate the particle size distribution to the entire solution. During a laser diffraction test, a laser is projected through a suspended cloud of particles and a collector oriented at 90° to the laser records the various laser deflections [3]. The amount of light collected at the collector element is used to determine the particle size distribution of a sample. Laser diffraction testing is widely accepted as an industry standard in testing aerosol particles, which are often desired to be in the size range of 1-10 μm [1,2].

The literature supports the assertion that bronchodilator dry drug particles (albuterol sulfate, ipratropium bromide, *etc.*) are most effective in controlling bronchospasms when in the size range of <10 μm [1]. Additionally, when a patient uses a personal metered dose inhaler (pMDI or MDI) the amount of albuterol deposited in the lungs rarely exceeds 20% with the majority of the medication "raining out" in the oropharyngeal airway [2]. Smaller particles have the added benefit of traveling more deeply into the lungs than larger particles and thus are highly desirable in dry drug aerosolized medications [1,2].

A Malvern laser diffraction system was used to quantify the particle size distribution reaching the end of an endotracheal tube (ETT) using various ETT adaptors. Also, particle size was determined for several adaptors and a MDI without use of an ETT. Below is the basic set-up used to collect data for the laser diffraction experiment.



Materials

- Malvern Laser Diffraction system
- Old prototype, new prototype, MDI, 60cc syringe, Bronchodilator Tee
- 8 mm I.D. ETT
- Albuterol sulfate HFA aerosol canister
- Styrofoam block, metal pipe, scotch tape
- Microsoft Excel for data compiling and computations

Methods

- Tests were performed both at the distal end of an ETT (Bronchodilator Tee, old prototype, new prototype, 60cc syringe) and without an ETT present (old prototype, new prototype, MDI)
- Set-up as shown above and test each adaptor of interest at least 3 times (some were tested 4) each to ensure repetitive, reliable data (n=3+). Prior to each test clear background noise due to other suspended in the sampling region
    - Each test ideally uses new ETT tube as well as a newly primed (5 actuations prior to test) canister of albuterol
    - Maintain proper ETT placement of 2.5 cm above incoming laser beam for all tests
- Export data as .txt files into Microsoft Excel and remove all time points where no data was collected, average percentage for each particle size, and plot percentage vs. particle size for each test

References

[1] Jones, S. A., G. P. Martin, and M. B. Brown. "High-pressure aerosol suspensions?A novel laser diffraction particle sizing system for hydrofluoroalkane pressurised metered dose inhalers." *International Journal of Pharmaceutics* 302.1-2 (2005): 154-65. *ScienceDirect*. Web. 4 Dec. 2009.

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Product design specification

Function:

The goal of this project is to make design changes to an endotracheal tube adaptor that was fabricated last semester for product optimization. The adaptor works as an interface to introduce aerosolized medication (e.g. Albuterol) from a pressurized canister into an anesthesia circuit to an intubated patient. This project was initiated due to a recent change in the Albuterol canister used by the UW-Hospital. The new canisters have been fitted with a non-removable, plastic, actuation counter resulting in a mechanical incompatibility with the old adaptor used at the hospital.

Last semester a prototype adaptor was produced that was universally compatible with all aerosolized medication canisters and also compatible with a specific gas sampling Luer port. It acts as a syringe to dispense medication in a simple fashion, with one hand, into the Luer port. This semester's objectives are: make the adaptor compatible with all Luer ports, adjust the size of the aperture at the distal end of the prototype for optimal medication delivery, and thoroughly test the prototype to ensure efficacy. The prototype will also be designed and constructed in a way such that it can be injection molded.

Client Requirements:

- Must be compatible with both new aerosolized medication canisters (with actuation counter) and with old style canisters (sans actuation counter).
- Should reliably deliver aerosolized medication to patient.
  - Particle size should be comparable or smaller than those observed last semester with Brochodilator Tee and patients Multi-Dosed Inhaler (MDI).
- The final prototype for this semester may be made of metal, however, the final design should be injection molded. The one time use, plastic adaptors should cost between $1.50-3.00 per unit.
- If metal, adaptor should be compatible with the hospitals cleaning solution, MetriCide.

- Must be compatible with all female Luer ports (distal 7.5mm of Luer port) on plastic, anesthesia elbows.
    - Must not disturb the 4-5L/min airflow from anesthesia circuit to patient.

1. Physical and Operational Characteristics

a.) Performance requirement: The device should consistently deliver Albuterol particles between 0.5-10μm in diameter to ensure maximum absorption by the lungs. The adaptor should work in conjunction with all styles of Albuterol canisters and should also be compatible with the distal 7.5mm of all female Luer ports. In addition, medication amount delivered should be at least 50% of the actuation amount (90μg).

b.) Safety: The adaptor must not restrict airflow of 4-5L/min through the circuit. Additionally, it must be fabricated with a sterile, medical-grade material. If made of plastic (HDPE), the adaptor should be able to withstand the force required to actuate the canister.

c.) Accuracy and Reliability: The adaptor should administer Albuterol droplets that range from 0.5-10μm in diameter. In addition, it should be comparable or exceed the particle size observed with the patient's hand-held MDI and the Bronchodilator Tee adaptor used by the hospital. The amount of Albuterol delivered should be at least 45μg per actuation.

d.) Life in Service: The adaptor can either be single-use and made of plastic (HDPE) or a reusable one made of metal (non-corrosive stainless steel or aluminum). If we opt for the reusable design, the adaptor should last for at least 5 year while undergoing sterilization with a solution such as MetriCide after each use.

e.) Shelf Life: The adaptor should be sterilely packaged and have a shelf life of at least 5 year.

f.) Operating Environment: The adaptor will be used almost exclusively in operating rooms at standard temperature and pressure by anesthesiologists and respiratory therapists. As such, there is no need to account for extreme temperatures, and there is little risk of the adaptor becoming dirty or contaminated.

g.) Ergonomics: The adaptor should friction fit into the first 7.5mm of a female Luer port with only a nominal force. All sharp edges of the existing prototype should be rounded off to maximize user safety. The housing area for the medication canister's nipple should be sized appropriately to form a snug fit between the nipple and the housing (3.1mm). The adaptor should be able to be comfortably used with one hand.

h.) Size: The prototype should fit the first 7.5mm of the female Luer port and should be kept at a maximum of 36mm wide by a maximum of 55mm long (this includes reducing the current length of the distal nozzle).

i.) Weight: There are no set limitations to the weight of the prototype, however the less the product weighs the better. This will be largely dictated by material choice.

j.) Materials: The prototype must be made of medical grade plastic, stainless steel, or aluminum and should also be compatible with MetriCide.

k.) Aesthetics/Appearance: The final product can be either transparent or a clear white color if plastic. Metal is also suitable as long as it does not interfere with medication or cleaning procedures.

2. Production Characteristics

a.) Quantity: One prototype for use by our client. Further production of additional units will be determined by our client and will be done via injection molding.

b.) Target Product Cost: The product should cost between $1.50-$3.00 if it is injection molded and disposable. Also, prototype re-design costs should be limited to $500.

3. Miscellaneous

a.) Standards and Specifications: Since the product we are designing will be used to create an opening in the ventilator circuit to allow aerosolized drugs to be administered during surgery, it will require FDA 501(k) approval if manufactured on a large scale. This device is related to the Bronchodilator Tee which was deemed substantially equivalent to nebulizer devices so 501(k)

approval should not be an issue. The device can be made out of medical-grade plastic or a light weight metal (aluminum). It must either be able to be mass-produced for one-time use or it must be able to withstand standard medical cleaning techniques (autoclaving or MetriCide). It also must be compatible with the propellant HFA (hydrofluoralkane), and if reusable it must be able to have a shelf life of 5 year.

b.) Consumer: Our client, Mark Schroeder, wants a reusable prototype that could be used as a basis for an injection-molded single-use adaptor. He does not have any preference with regards to the material used to fabricate the adaptor as long as it is medically safe. General modifications he would like made to our current prototype include: orifice size change, rounded corners, shortened nozzle/punch out and replace nozzle, addition of actuation counter stud, and FDA 501(k) approval.

c.) Patient-Related Concerns: Any material used on the device will have to withstand repeated exposure to the HFA propellant without chipping or flaking off into the patient's lungs. The particle size should consistently fall within the above mentioned range to ensure patient safety. This device will be used exclusively by trained, licensed medical professionals.

d.) Competition: The need for our device arose when drug companies were forced to switch aerosolized drug propellants from CFC's (chlorofluorocarbons) to HFA's (hydrofluoroalkanes) because the CFC's were dispersing ozone-depleting reagents into the atmosphere. Along with the switch in propellant, some companies also redesigned their canisters, making them incompatible with the current adaptors due to a non-removable actuation counter cap. The market for MDI adaptors is very large and diverse, but most of these products are compatible with the old canisters (those lacking the actuation counter cap). There are several patented devices that are similar to ours, but slight differences in design make our product unique. US Patent #7207329 is an adaptor for both a syringe and MDI into the ventilator circuit, but since our product will not require an adaptor for a syringe our final design will be noticeably different. The hospital currently uses the Bronchodilator Tee designed by Boehringer Labs (US Patent #D294298). Nebulizers also exist that can be used to atomize Albuterol, but these are much different in form and function from our device and have significant patient-related safety

concerns. Other aerosolize delivery devices include US Patent #2003/0150462, US Patent #6014972, US Patent #7207329B2, US Patent #3667475, and US Patent #3104062, however, these devices do not adequately meet the needs of our client.